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- (72) Inventors: LAPIDUS, Stanley, N.; 12 Old Evergreen Road, Bedford, NH 03110 (US). SHUBER, Anthony, P.; 11 Grant Street, Milford, MA 01757 (US). For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



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(54) Title: METHODS FOR IMPROVING SENSITIVITY AND SPECIFICITY OF SCREENING ASSAYS

(57) Abstract: Methods of the invention comprise assays for markers indicative of cancer or precancer. Assays of the invention are performed on samples obtained from a patient by non-invasive or minimally-invasive methods. The invention provides nucleic acid indicia of cancer or precancer with high sensitivities and high specificities for detection.

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According to International Patent Classification (IPC) or to both national classification and IPC

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C120

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used):

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, MEDLINE, BIOSIS, EMBASE

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SIDRANSKY DAVID: "Nucleic acid-based methods for the detection of cancer." SCIENCE (WASHINGTON D C), vol. 278, no. 5340, 7 November 1997 (1997-11-07), pages 1054-1058, XP002170462 ISSN: 0036-8075	1-8, 15-17, 20-24, 29-33
Y	page 1054 -page 1057; table 1 ---	9-14
Y	WO 95 00669 A (PHARMACIA BIOTECH AB ;BAYLOR COLLEGE MEDICINE (US); CASKEY C THOMA) 5 January 1995 (1995-01-05) page 14, line 1 - line 28; claims 1-18 --- -/--	9-14

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/07882

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	VET JACQUELINE A M ET AL: "Comparative analysis of p53 mutations in bladder washings and histologic specimens." AMERICAN JOURNAL OF CLINICAL PATHOLOGY, vol. 110, no. 5, November 1998 (1998-11), pages 647-652, XP001009905 ISSN: 0002-9173 page 650, right-hand column -page 652, left-hand column ---	1,6,8, 16,17, 22-25,32
X	CAWKWELL L ET AL: "Frequency of allele loss of DCC, p53, RBI, WT1, NF1, NM23 and APC/MCC in colorectal cancer assayed by fluorescent multiplex polymerase chain reaction." BRITISH JOURNAL OF CANCER, vol. 70, no. 5, 1994, pages 813-818, XP001009897 ISSN: 0007-0920 page 817; figure 2 ---	1-6, 15-17, 22-24, 22,33
X	WO 96 29430 A (WAYNE JOHN CANCER INST ;NAT GENETICS INST (US)) 26 September 1996 (1996-09-26) claims 1-20 ---	1,8,16, 17, 22-24,32
X	DE 197 36 691 A (GIESING MICHAEL PROF DR MED) 25 February 1999 (1999-02-25)  claims 1-4 ---	1-8, 15-17, 20-24, 32,33
A	HOANG JEAN-MARC ET AL: "BAT-26, an indicator of the replication error phenotype in colorectal cancers and cell lines." CANCER RESEARCH, vol. 57, no. 2, 1997, pages 300-303, XP002162454 ISSN: 0008-5472 page 300 -page 302 -----	18,19

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/07882

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9500669 A	05-01-1995	SE 501439 C	13-02-1995
		AT 185843 T	15-11-1999
		AU 698553 B	29-10-1998
		AU 7212194 A	17-01-1995
		DE 69421277 D	25-11-1999
		DE 69421277 T	31-05-2000
		EP 0705349 A	10-04-1996
		EP 0969103 A	05-01-2000
		ES 2141828 T	01-04-2000
		JP 9501312 T	10-02-1997
		SE 9302152 A	23-12-1994
		US 6153379 A	28-11-2000
WO 9629430 A	26-09-1996	AU 5310296 A	08-10-1996
		EP 0871768 A	21-10-1998
		US 6057105 A	02-05-2000
DE 19736691 A	25-02-1999	WO 9910528 A	04-03-1999
		EP 1007740 A	14-06-2000

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